REMARKS - General

This is responsive to the Examiner's Office Action mailed November 16, 2007. Applicants have amended claims 1, 15, and 17; have cancelled claims 2-14, 16, and 18-41. Thus claims 1, 15, and 17 (a total of 3 claims, including 1 independent claim) are pending in this application.

The status of all claims and the text of all pending claims are shown above. In the changes made to the claims by the current amendment, ~~deletions are shown by strikethrough~~, and additions are underlined.

Discussion of Inventorship

Applicants certify that the subject matter of the various claims in this patent application was commonly owned at the time any invention covered therein was made absent any evidence to the contrary.

Discussion of Claims Rejections - 35 USC §112

The Examiner rejected claims 1-4, 7-9 and 11-20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

- Claim 1 is drawn to a medical device where the medical device also comprises, in pertinent part, a biodegradable apparatus. Claim 1 has been amended to recite "a biodegradable stent" to overcome the §112 claim rejection.
- Claim 1 is drawn, in pertinent part, to a medical device that comprises a "crosslinking agent". The examiner cited that the specification is written broadly simply advising of "a crosslinker, such as genipin, its derivatives, analog, stereoisomers and mixtures thereof" and the listing of this non-exacting reference is insufficient to meet the written description provision of 35 U.S.C. 112, first paragraph.
- Applicants submit that, firstly, the crosslinking agent has been defined in paragraph [0042] as to indicate a chemical agent that could **crosslink two molecules**. Further, the crosslinking agent of genipin, its structure, and its manufacturing method have been fully disclosed in details as in paragraph [0050]:

"*Genipin, shown in Structure I of FIG. 2A, is an iridoid glycoside present in fruits (Gardenia jasmindides Ellis). It may be obtained from the parent compound geniposide, Structure II (FIG. 2B), which may be isolated from natural sources as described in elsewhere. Genipin, the aglycone of geniposide, may be prepared from the latter by oxidation followed by reduction and hydrolysis or by enzymatic hydrolysis. Alternatively, racemic genipin may be prepared synthetically. Although Structure I shows the natural configuration of genipin, any stereoisomer or mixture of stereoisomers of genipin as shown later may be used as a crosslinking reagent, in accordance with the present invention.*" The genipin derivatives and/or genipin analog may have the chemical formulas (Formula 1 to Formula 4 in the instant invention) and fully disclosed in paragraphs [0054] to [0077]. Applicants submit that the crosslinking agent of genipin has been sufficiently and completely disclosed.

- Claim 1 has been amended to recite "a biodegradable stent, comprising: at least one bioactive agent; and chitosan biological material, said biological material comprising said at least one bioactive agent, wherein said biological material ***is crosslinked with a crosslinking agent*** ....". However, claim 1 does not recite "a medical device that comprises a "crosslinking agent"; instead, claim 1 recites "a ***biodegradable stent that has been treated with*** a crosslinking agent."
- It is understandable that a 'crosslinking agent' is involved in modifying the chemical structure of the raw molecules that are crosslinked later. The 'crosslinking agent' is neither an additive, nor a drug; and has no pharmaceutical efficacy after being used up in the crosslinking process.

Double Patenting

Claims 1-4, 7-9 and 11-20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent Application No. 10/520,878. A timely filed terminal disclaimer (for 10/520,878, 11/130,787, 10/929,047, 10/906,239, 10/811,413, 10/916,170, and 10/827,673 as USP 7,101,857) in compliance with 37

CFR 1.321 (c) is included to overcome an actual or provisional rejection based on a nonstatutory double patenting ground.

Discussion of Claims Rejections - 35 USC §102(b)

The Examiner rejected claims 1, 4, 8-9, 11-12, 16, and 18-20 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,500,013 to Buscemi et al.

Buscemi et al. disclose a history of stent development, using certain materials (no chitosan biological material), stent formation, copolymerization, etc. The invention in Buscemi et al is a biodegradable stent, saturated with drugs, that has a matrix strengthened by, for example, polylactic acid (not crosslinked with a crosslinking agent of genipin or an epoxy compound or with ultraviolet irradiation as taught in the instant invention). Buscemi et al also disclose that drugs are incorporated into the stent. However, Buscemi et al does not teach a biodegradable stent made of chitosan biological material that is crosslinked (chemically treated or via ultraviolet irradiation). Buscemi et al stent does not possess the novel properties that "enables the resulting material with **less antigenicity or immunogenicity**" due to unique feature of crosslinking of the instant invention (enabling specification cited from paragraph [0003] of the instant invention) because Buscemi et al. stent is not crosslinked.

Claim 1 has been amended to recite "A biodegradable stent, comprising: at least one bioactive agent; and chitosan biological material that is crosslinked".

- The "chitosan-drug-genipin compound" is disclosed & supported by paragraph [0085].
- The "chitosan source" is disclosed & supported by paragraph [0154].
- Paragraph [0167] recites "Special features for the ..... drug-loaded chitosan crosslinked by genipin may be characterized by: the crosslinked collagen/chitosan with interpenetrated drug enables drug diffusion at a controlled rate;.... The whole process for manufacturing ..... chitosan-drug-genipin compound can be automated in an environmentally controlled facility....".

Applicants respectfully request reconsideration of claim rejection (claim 1) as disclosed above. Claims 4, 8-9, 11-12, 16 and 18-20 have been cancelled.

Discussion of Claims Rejections - 35 USC §103(a)

The Examiner rejected claims 2, 3, 13 and 15 as being unpatentable over Buscemi et al in view of U.S. Patent No. 5,272,172 to Fujii et al. as evidenced by Vaya, Ampara, et al. in 15 October 1993, *Thrombosis Research*, Vol. 72, Issue 2, pages 119-126.

Fujii et al teach that "Cape Jasmim (jasminoides Ellis)... has long been known to have pharmacological effects such as an anti-arteriosclerosis agent, a blood coagulation inhibitor and a cholagogue, and geniposide as a typical active component of Cape Jasmine". The examiner cites that " Due to the overlapping subject matter of treating atherosclerotic and hyperlipidemic conditions resultant from erythrocyte aggregation, one of ordinary skill in the art would be motivated to combine the teachings of Buscemi et al with the teachings of Fujii et al to conclude that a biodegradable stent with medications containing genipin or an epoxy compound, or a biological material to treat hypercholesterolemia would be prima facie obvious over prior art."

Applicants submit that Cape Jasmine is not a crosslinking agent (as per USP 5272172 or USP 5459160 by Fujii et al); instead, Cape Jasmine functions as a drug that might saturate the stent of Buscemi et al. In the instant invention, a crosslinking agent of genipin or an epoxy compound does not exist as an added drug to said biodegradable stent of chitosan bases, There is no residual crosslinking agent (to function as a drug as taught by Fujii et al.) since the degree of crosslinking is not 100%; the residual genipin or epoxy compound, if any during the manufacturing process, was washed away or removed from the final biodegradable stent. Rather, the genipin or epoxy compound took part in forming a new crosslinked biomolecule that results in **less antigenicity or immunogenicity.**

Cape jasmine has different chemical structure or properties as compared to genipin or epoxy compounds, which are purely categorized as "crosslinking agent" to crosslink chitosan biological material of the biodegradable stent of the present invention. Genipin or epoxy compounds do not exert any pharmaceutical effects to the biodegradable stent. In summary, neither Buscemi et al, Fujii et al, nor combination whatsoever has disclosed a biodegradable stent made of chitosan biological material that is crosslinked and enclosed at least one bioactive agent (for example, drugs, growth factors or cell type). The subject matter (mostly non-drug type bioactive agents) in claim 15 "ApoA-I Milano or recombinant ApoA-I Milano/phospholipid

complexes" and in claim 17 "lipostabil" are unobvious with regard to Buscemi et al., Fujii et al., Vaya et al., or combinations thereof.

Applicants respectfully request reconsideration of claim rejection (claims 1, 15 and 17) as disclosed above.

Conclusion and Conditional Request For Constructive Assistance

For all of the above reasons, applicants submit that claims are now in proper form, and that the claims all define patentably over the prior art. Therefore, they submit that this application is now in condition for allowance, which action they respectfully solicit. If, for any reason, this application is not believed to be in full condition for allowance, applicants respectfully request the constructive assistance and suggestions of the Examiner pursuant to M.P.E.P. § 706.03(d) and § 707.07(j) in order that the undersigned can place this application in allowable condition as soon as possible and without the need for further proceedings. If further issues remain to be resolved, the Examiner is cordially invited to contact the undersigned (949-887-2966) such that any remaining issues may be promptly resolved.

Respectfully submitted,

Hosheng Tu 12-19-2007

Hosheng Tu, applicant Date